Claims

1. An isolated polypeptide wherein said polypeptide is represented by the amino acid sequence as shown in Figure 1a, or a variant polypeptide which variant is modified by addition, deletion or substitution of at least one amino acid residue characterised in that said polypeptide has the following characteristics:

   i) a polypeptide which preferentially binds the tumour suppressor polypeptide p53 to inhibit the pro-apoptotic activity of p53 when compared to a polypeptide, or variant thereof, as represented by the amino acid sequence as shown in Figure 2a;

   ii) a polypeptide which includes at least one amino acid residue which residue is ubquitinated; and

   iii) a polypeptide which comprises an amino-terminal polypeptide domain wherein said domain is represented between amino acid 1 and 483 of the amino acid sequence shown in Figure 1a.

2. A polypeptide according to Claim 1 wherein said polypeptide preferentially binds p53 when compared to a polypeptide represented by the amino acid sequence shown in Figure 2a.

3. A polypeptide according to Claim 1 or 2 wherein said polypeptide is modified by addition, deletion or substitution of at least one amino acid residue wherein said modification is between amino acid residues 1 and 483 of the amino acid sequence presented in Figure 1a.

4. A polypeptide according to any of Claims 1-3 wherein said polypeptide comprises the amino acid sequence shown in Figure 1a.

5. A polypeptide according to any of Claims 1-4 wherein said polypeptide consists of the amino acid sequence shown in Figure 1a.

6. An isolated nucleic acid molecule wherein said nucleic acid molecule encodes a polypeptide according to any of Claims 1-5.

7. An isolated nucleic acid molecule according to Claim 6 wherein said nucleic acid molecule is represented by the nucleic acid sequence shown in Figure 1b or a nucleic acid molecule which hybridises to the sequence shown in Figure 1b, under stringent hybridisation conditions, and which encodes a polypeptide according to any of Claims 1-5.

8. A nucleic acid molecule according to Claim 6 or 7 wherein said nucleic acid molecule consists of the nucleic acid sequence shown in Figure 1b.

9. A nucleic acid molecule according to any of Claims 6-8 wherein said molecule is a cDNA.

10. A nucleic acid molecule according to any of Claims 6-8 wherein said molecule is genomic DNA.

11. A vector comprising a nucleic acid molecule according to any of Claims 6-10.

12. A method for the production of the polypeptide according to any of Claims 1-5, comprising the steps:

i) providing a cell transformed/transfected with a nucleic acid molecule or vector according to any of Claims 6-11;

ii) growing said cell in conditions conducive to the manufacture of said polypeptide; and

iii) purifying said polypeptide from said cell, or its growth environment.

13. An antibody, or binding fragment thereof, which binds the polypeptide according to any of Claims 1-5 characterised in that said antibody binds said polypeptide between amino acid residues 1 to 483 of the amino acid sequence shown in Figure 1a.

14. An antibody according to Claim 13 wherein said fragment is a Fab fragment.

15. An antibody fragment according to Claim 14 wherein said antibody is selected from the group consisting of: $F(ab')_2$, Fab, Fv and Fd fragments; and antibodies comprising CDR3 regions.

16. An antibody, or binding fragment thereof, according to any of Claims 13-15 wherein said antibody is a humanised.

17. An antibody, or binding fragment thereof, according to any of Claims 13-15 wherein said antibody is a chimeric antibody.

18. A polypeptide according to any of Claims 1-5 for use as a pharmaceutical.

19. A nucleic acid molecule or vector according to any of Claims 6-11 for use as a pharmaceutical.

20. Use according to Claim 19 wherein said nucleic acid molecule is an inhibitory RNA molecule.

21. Use according to Claim 19 wherein said nucleic acid molecule is an antisense nucleic acid molecule.

22. Use according to Claim 20 or 21 wherein said nucleic acid molecule is selected from the group consisting of an antisense molecule or an inhibitory RNA molecule designed with reference to the nucleic acid sequence shown in Figure 3, wherein said antisense or inhibitory RNA molecule is designed to that part of said nucleic acid sequence which encodes amino acid residue 1 to 483 defined as shown in Figure 1a.

23. Use according to Claim 22 wherein said nucleic acid molecule is provided as a transcription cassette comprising an nucleic acid sequence operatively linked to a promoter which promoter transcribes said nucleic acid molecule to produce an antisense nucleic acid molecule, said sequence selected from the group consisting of:

i) a nucleic acid sequence, or part thereof, as represented in Figure 1b;

ii) a nucleic acid sequence which hybridises to the sense sequence presented in Figure 1b and which encodes a polypeptide according any of Claims 1-6.

24. Use according to Claim 22 wherein said nucleic acid molecule is provided as a transcription cassette comprising a nucleic acid molecule, or part thereof, selected from the group consisting of:

i) a nucleic acid molecule represented by the nucleic acid sequence in Figure 1b;

ii) a nucleic acid molecule which hybridises to the sequence in (i) above and which encodes a polypeptide according to any of Claims 1-5; or

iii) a nucleic acid molecule which is degenerate because of the genetic code to the sequences defined in (i) and (ii) above; wherein said cassette is adapted such that both sense and antisense nucleic acid molecules are transcribed from said cassette.

25. Use according to Claim 24 wherein said cassette is provided with at least two promoters adapted to transcribe both sense and antisense strands of said nucleic acid molecule.

26. Use according to Claim 24 wherein said cassette comprises a nucleic acid molecule wherein said molecule comprises a first part linked to a second part wherein said first and second parts are complementary over at least part of their sequence and further wherein transcription of said nucleic acid molecule produces an RNA molecule which forms a double stranded region by complementary base pairing of said first and second parts.

27. Use according to Claim 26 wherein said first and second parts are linked by at least one nucleotide base.

28. Use according to any of Claims 23-27 wherein said cassette is part of a vector.

29. A screening method to identify an agent which modulates the interaction of a p53 binding protein with a p53 polypeptide wherein said method comprises the following steps of:

i) forming a preparation comprising a polypeptide according to any of Claims 1-5 and a p53 polypeptide, or sequence variant thereof, and at least on agent to be tested;

iii) determining the activity of said agent with respect to the binding of said polypeptide to said p53 polypeptide.

30. A screening method for the identification of an agent which modulates the interaction of a Bcl-2 binding polypeptide with a Bcl-2 polypeptide wherein said method comprises the steps of:

i) forming a preparation comprising a polypeptide as represented by the amino acid sequence shown in Figure 2a, or a variant polypeptide which is modified by addition deletion or substitution of at least one amino acid residue and a Bcl-2 polypeptide, or variant thereof, and at least one agent to be tested; and

iii) determining the activity of said agent with respect to the binding of said polypeptide to said Bcl-2 polypeptide.

31. A screening method to identify agents which modulate the ubquitination of a polypeptide comprising the steps of:

i) forming a preparation comprising a polypeptide according to any of Claims 1-5, a ubiquitin polypeptide or variant thereof, polypeptide(s) with the specific activity associated with ubiquitin conjugating polypeptides and at least one agent to be tested;

ii) determining the activity of said agent with respect to the conjugation of ubiquitin to said polypeptide.

32. A method according to any of Claims 29-31 wherein said agent is a peptide or polypeptide.

33. A method according to Claim 32 wherein said peptide/polypeptide is an antibody or antibody binding fragment.

34. A method according to any of Claims 29-31 wherein said agent is an aptamer.